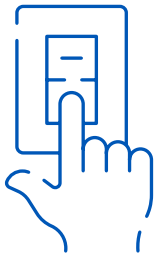


Understanding the KRAS G12D Mutation

THE MOST COMMON KRAS MUTATION IN HUMAN CANCERS



What is KRAS?

KRAS (pronounced KAY-rass) is a gene found in all human cells. Normally, the KRAS gene produces a protein that acts as an “ON/OFF” switch for pathways that relay signals to control how cells grow, mature, proliferate, and die. When the KRAS gene is mutated (changed at the DNA level), it can act as an oncogene (a gene that promotes cancer development and growth). **The protein produced by the mutated KRAS gene becomes stuck in the “ON” position, causing cells to grow and divide uncontrollably and form tumors that can become aggressive cancers.**

KRAS is one of the most commonly mutated genes in human cancers. There are several distinct KRAS mutations that can lead to cancer, including KRAS G12D, KRAS G12C, and KRAS G12R. These mutations differ in how they affect the structure and function of proteins, how common they are in the human population, which type of cancer they are most likely to be found in, and how they respond to therapy, but they can all act as key drivers of cancer development and growth.

What is the KRAS G12D mutation?

Different types and locations of tumors can be caused by different mutations in the genes that control cell growth and division.

KRAS G12D is the most common KRAS mutation in human cancers, accounting for

26% OF ALL KRAS MUTATIONS.

Each year in the U.S.

61K PATIENTS WITH METASTATIC CANCER
are diagnosed with a KRAS G12D mutation.



The name “KRAS G12D” describes a specific change at a precise spot on the KRAS protein. “**G12**” refers to the 12th position in the protein, and “**D**” means that one building block of the protein has been replaced by another. **This small change can have a big impact on how cancer cells grow and survive.**

Pancreatic cancer, colorectal cancer (CRC), and non-small cell lung cancer (NSCLC) are among the most common types of cancer that are typically driven by the KRAS G12D mutation.

Is my cancer driven by a KRAS G12D mutation?

Many people do not know the mutation status of their tumor.

The specific genomic makeup of a tumor can be determined by genomic testing (also called molecular or biomarker testing). To detect KRAS G12D, pathologists perform genomic testing on a tissue sample taken from a tumor biopsy or surgical removal of the tumor. A blood sample from the patient (called a liquid biopsy) also can be used.

Testing involves reading the tumor’s DNA to detect cancer-causing mutations.

2 ROUTES TO TESTING



TISSUE



BLOOD



Why is genomic testing important?

Knowing if your tumor has a specific mutation— such as KRAS G12D—is important for several reasons. It can help your doctor:

- ✓ Understand if your cancer may respond to a specific type of treatment
- ✓ Develop a personalized treatment plan given the specific genomic makeup of your tumor
- ✓ Decide if you might be able to benefit from a therapy that specifically targets KRAS G12D
- ✓ Better understand your prognosis

What treatment options are available for cancers that have the KRAS G12D mutation?

For many years, KRAS was considered “undruggable,” meaning scientists believed it was not possible to design medicines that could directly block its cancer-driving signals. Currently, there are no treatments specifically targeting KRAS G12D approved by the U.S. Food and Drug Administration (FDA).

For patients with advanced solid tumors that harbor the KRAS G12D mutation, treatment options may include:



SURGERY



CHEMOTHERAPY



IMMUNOTHERAPY



TARGETED THERAPY



RADIOTHERAPY



CLINICAL TRIAL STUDYING INVESTIGATIONAL TREATMENTS



The TARGET-D Clinical Trial Program is evaluating an investigational medicine, VS-7375, to treat certain types of solid tumors that harbor a KRAS G12D mutation. The Phase 1/2 clinical trial is being conducted to determine the appropriate dose of the medicine and evaluate how well-tolerated it is to give to people both alone and in combination with other treatments. VS-7375 is also being studied in three TARGET-D Phase 2 clinical trials to evaluate the safety, tolerability and efficacy (how well it works to reduce your tumors) in pancreatic, non-small cell lung cancer, and colorectal cancer.

Talk to your doctor to learn if a clinical trial specifically targeting the **KRAS G12D mutation** might be right for you.

For more information on the TARGET-D Clinical Trial Program, you can also visit [verastem.com/clinical-trials](https://www.verastem.com/clinical-trials)